DOCKET NO.: ALZA-0022 (ARC-2865-R3) **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Johan H. Geerke and Steven F. Stone** Confirmation No.: **1409**

Serial No.: **09/324,343** Group Art Unit: **1617**

Filing Date: **June 2, 1999** Examiner: **Chong, Yong Soo**

For: **Methods And Apparatus For Determining Formulation Orientation Of Multi-Layered Pharmaceutical Dosage Forms**

Mail Stop Appeal-Brief Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

APPELLANT'S BRIEF PURSUANT TO 37 C.F.R. § 41.37

This brief is being filed in support of Appellant's appeal of the rejections of claims 18, 20, 32-33, and 35-36 dated January 17, 2007. A Notice of Appeal was filed on July 17, 2007. Appellant herein withdraws the appeal with respect to the rejection of claim 38.

1. REAL PARTY IN INTEREST

The real party in interest is Alza Corporation, a U.S. corporation having its principal office at 950 Page Mill Road, Palo Alto, CA 94303-0802.

2. RELATED APPEALS AND INTERFERENCES

No related appeals or interferences are pending.

3. STATUS OF CLAIMS

Pending	:	Claims 1 to 38
Rejected	:	Claims 18-20, 32-33, 35-36, and 38
Objected to	:	Claims 34 and 37
Allowed	:	None

Withdrawn	:	Claims 1-17 and 21-31
Appealed	:	Claims 18-20, 32-33, and 35-36
Appeal Withdrawn	:	Claim 38.

4. STATUS OF AMENDMENTS

No claim amendments were filed subsequently to the final rejection dated January 17, 2007.

5. SUMMARY OF CLAIMED SUBJECT MATTER

The claimed inventions are generally directed to methods of making multi-layer tablet dosage forms and detecting their orientation.

Independent claim 18 is directed to methods of making a three-layer capsule-shaped tablet comprising: formulating a drug-containing first layer and a drug-containing second layer, wherein one of the layers comprises a first colorant; formulating a non-drug-containing third layer comprising a second colorant; compressing the layers into a capsule-shaped tablet; and detecting the formulation orientation of the tablet with a color detector. *See* specification at page 9, line 27 to page 15, line 7; page 21, line 18 to page 22, line 7.

Independent claim 20 is directed to methods of making a three-layer capsule-shaped tablet comprising: formulating a drug-containing first layer and a drug-containing second layer, wherein the second layer comprises a first colorant; formulating a non-drug-containing third layer comprising a second colorant; compressing the layers into a capsule-shaped tablet; and detecting the formulation orientation of the tablet with a color detector. *See* specification at page 9, line 27 to page 15, line 7; page 22, lines 11-29.

6. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The issue on appeal is as follows:

- Whether or not those of ordinary skill in the art would have found the inventions recited in claims 18-20, 32-33, and 35-36 to have been obvious

over U.S. Pat. No. 5,248,310 to Barclay, *et al.* ("the Barclay patent") in view of U.S. Pat. No. 5,785,994 to Wong, *et al.* ("the Wong patent") in further view of U.S. Pat. No. 5,294,770 to Riddle, *et al.* ("the Riddle patent").

7. ARGUMENT

The inventions recited in claims 18-20, 32-33, and 35-36 would not have been obvious to those of ordinary skill because combination of the respective teachings of the cited patents, even if motivated, would not have produced any claimed invention.

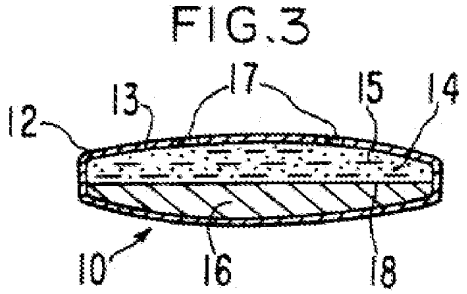
The dosage form produced in accordance with independent claim 18 comprises "a three-layer capsule-shaped tablet" wherein the first layer "contain[s] a drug ingredient" and wherein the second layer also "contain[s] a drug ingredient" (*see* CLAIMS APPENDIX at claim 18). The first layer "is located at one end of the capsule-shaped osmotic tablet and the third layer is located at the other end of the capsule-shaped osmotic tablet and the second layer is located between the first layer and the third layer" (*See id.*). The capsule-shaped osmotic dosage form produced in accordance with claim 18 is therefore a three-layer capsule-shaped dosage form having a drug/drug/no drug orientation.

The dosage form produced in accordance with independent claim 20 also comprises "a three-layer capsule-shaped tablet" wherein the first layer "contain[s] a drug ingredient" and wherein the second layer also "contain[s] a drug ingredient" (*see* CLAIMS APPENDIX at claim 20).). The first layer "is located at one end of the capsule-shaped osmotic tablet and the third layer is located at the other end of the capsule-shaped osmotic tablet and the second layer is located between the first layer and the third layer" (*See id.*). The capsule-shaped osmotic dosage form produced in accordance with claim 20 is therefore a three-layer capsule-shaped dosage form having a drug/drug/no drug orientation.

Although the Examiner summarily contends that "combination of the cited references does indeed form a drug/drug/no drug orientation three layer tablet structure" (1/17/07 Final Rejection at page 7), the Examiner has failed to identify any evidence or rationale supporting the contention. It is undisputed, for example, that neither the Wong patent nor the Barclay

patent disclose or suggest a three-layer dosage form in which multiple drug-containing layers are compressed together. [1]

The Barclay patent discloses a two-layer dosage form with a *single* drug-containing layer. Figure 3 of the Barclay patent depicts representative dosage form 10 featuring a wall 12, a first layer of beneficial agent 14, and a second layer 16 consisting of an expandable driving member (*see* Barclay patent at col. 6, lines 16-45 & FIG. 3). Figure 3 of the Barclay patent is reproduced below:



This dosage form does not comprise a three-layer structure.

The Wong patent discloses a three-layer dosage form containing a *single* drug-containing layer and optionally including a drug-containing outer coating. Figure 4 of the Wong patent depicts representative dosage form 10 featuring a wall 12, a drug-free first layer 18, a second layer 22 consisting of a drug 15, and a third, push layer 24 comprising an osmopolymer "that exhibits fluid imbibation properties" (*see* Wong patent at col. 5, lines 21-32; col. 9, lines 38-40; col. 12, lines 40-44, describing the components of the dosage form depicted in Figure 3; the components are not separately described with respect to Figure 4)). Figure 4 also includes an external coat 14 that releases drug 15 when dissolved (*see* Wong patent at col. 2, lines 41-57, describing the components of the dosage form depicted in Figure 2, which are not separately described with respect to Figure 4). Figures 2-4 of the Wong patent are reproduced below:

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[1] The Examiner does not contend that the Riddle patent discloses drug layers but, rather, that it discloses the use of a color detector to orient a tablet during the manufacturing process (*see, e.g.,* 1/17/07 Final Rejection at page 6 & 5/11/07 Advisory Action at PTO-303 Continuation Sheet).

FIG.2

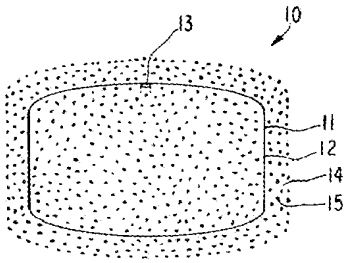


FIG.3

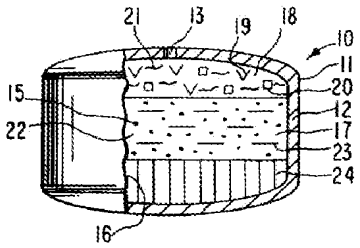
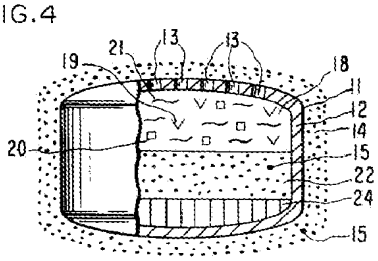


FIG.4



This dosage form does not comprise a three-layer capsule-shaped osmotic dosage form with more than a single drug-containing layer.

Although the Examiner contends that "Wong teaches a three or more layered tablet that provides a varying pattern of drug release" (1/17/07 Final Rejection at page 7), one of the structures in the Wong patent upon which the Examiner relies is the drug-containing overcoat, *i.e.,* element 14 in FIGS. 2 and 4 of the Wong patent (*see also* col. 17, lines 34-47). Because this overcoat does not correspond to any of the claimed layers (at least because it is not suitable to be compressed into a capsule-shaped osmotic tablet), the Examiner's proposed combination of references, even if motivated, would not have produced any claimed invention. For at least this reason, the rejection of the pending claims under § 103(a) is improper and should be withdrawn. 35 U.S.C. § 103(a) ("A patent may not be obtained . . . if the differences between the subject matter sought to be patented and the prior art are such that *the subject matter as a whole* would have been obvious . . .") (emphasis added); *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974) (all limitations set forth in a patent claim must be taught or suggested in the prior art to establish a *prima facie* case of obviousness); M.P.E.P. § 2143.03.

To the extent that the Examiner attempts to establish obviousness by merely alleging that Appellants' inventions would have been "well within the level of an [sic] ordinary skill in the art" (1/17/07 Final Rejection at page 7), the patent laws require much more than such a bare allegation. Indeed, it is well established that an allegation of obviousness that lacks objective support is improper. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1734, 167 L. Ed. 2d 705, 715 (U.S. 2007) (the analysis supporting a rejection under 35 U.S.C. § 103(a) should be made explicit, and it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements" in the

manner claimed); *Ex parte Levengood*, 28 U.S.P.Q.2d 1300 (Bd. Pat. App. & Inter. 1993); *In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000). Because the Examiner failed to identify any objective evidence that it would have been obvious (or even possible) to modify the teachings of the prior art in a way that would have produced the three-layer, drug/drug/no drug orientation of the present invention, the level of skill in the art is simply irrelevant.

Conclusion

Because there is no reason to believe that combination of the cited references would have produced any claimed invention, Appellants request that this patent application be remanded to the Examiner with an instruction to withdraw the rejection of claims 18-20, 32-33, and 35-36 under 35 U.S.C. § 103(a).

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CLAIMS APPENDIX

The following claims are involved in the present appeal:

18. A method of making a three-layer capsule-shaped tablet comprising:

formulating a first layer containing a drug ingredient and a second layer containing a drug ingredient, wherein one of the layers comprises a first colorant;

formulating a non-drug ingredient containing third layer comprising a second colorant that is distinguishable from the first colorant or from no color and not containing any drug ingredient;

compressing the first, second and third layers into a capsule-shaped osmotic tablet wherein the first layer is located at one end of the capsule-shaped osmotic tablet and the third layer is located at the other end of the capsule-shaped osmotic tablet and the second layer is located between the first layer and the third layer such that the formulation orientation of the tablet can be determined by detecting the color at a spot location on a side of the tablet corresponding to one or another differently-colored layer depending on the formulation orientation of the tablet; and

detecting the formulation orientation of the tablet with a color detector directed at a spot location on the side of the tablet.

19. The method of claim 18 wherein the first colorant is light and the second colorant is dark.

20. A method of making a three-layer capsule-shaped tablet comprising:

formulating a first layer containing a drug ingredient and not containing any colorant;

formulating a second layer containing a drug ingredient and a first colorant, the first colorant being complementary to no color;

formulating a third layer containing a second colorant that is distinguishable from the first colorant or from no color and not containing any drug ingredient;

compressing the first, second and third layers into a capsule-shaped osmotic tablet the first layer is located at one end of the capsule-shaped osmotic tablet and the third layer is located at the other end of the capsule-shaped osmotic tablet and the second layer is located

between the first layer and the third layer such that the formulation orientation of the tablet can be determined by detecting the color at a spot location on a side of the tablet corresponding to one or another differently-colored layer depending on the formulation orientation of the tablet; and

detecting the formulation orientation of the tablet with a color detector directed at a spot location in the side of the tablet.

21.- 31. (Withdrawn)

32. The method of claim 18 wherein said second layer comprises a larger concentration of drug ingredient than said first layer.

33. The method of claim 18 wherein said first and second layers comprise methylphenidate chloride.

34. The method of claim 18 wherein said first layer comprises about 9% to about 10% by weight methylphenidate chloride and said second layer comprises about 13% to about 14% by weight methylphenidate chloride.

35. The method of claim 20 wherein said second layer comprises a larger concentration of drug ingredient than said first layer.

36. The method of claim 20 wherein said first and second layers comprise methylphenidate chloride.

37. The method of claim 20 wherein said first layer comprises about 9% to about 10% by weight methylphenidate chloride and said second layer comprises about 13% to about 14% by weight methylphenidate chloride.

38. A method of making a multi-layer tablet comprising:

adding a first colorant to one formulation layer containing a drug ingredient proximately positioned at a dispensing end of the multi-layered tablet, the first colorant being complementary to no color;

adding a second colorant to at least one formulation layer not containing any drug ingredient proximately positioned at a push end of the multi-layered tablet, the second colorant distinguishable from the first colorant or from no color;

compressing the formulation layers into a capsule-shaped osmotic tablet such that the formulation orientation of the tablet can be determined by detecting the color at a spot location on a side of the tablet corresponding to one or another differently-colored formulation layer depending on the formulation orientation of the tablet, and

detecting the formulation orientation of the tablet with a color detector directed at a spot location on a side of the tablet.

EVIDENCE APPENDIX

No additional evidence is submitted in the Evidence Appendix.

RELATED PROCEEDINGS APPENDIX

No related appeals or interferences are pending.